

Scientific Abstract

A Randomized Phase II Study of Ad5CMV-p53 plus Radioactive Seed Implant vs Seed Implant Alone for PSA Relapse after External Beam Radiotherapy for Prostate Cancer

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A rising PSA after external beam radiotherapy for patients with clinically localized prostate cancer is usually representative of local persistence of disease. Those with a negative metastatic work-up are left with four options: 1) observation, 2) androgen ablation alone, 3) salvage prostatectomy, or 4) salvage brachytherapy. The first two options are palliative. Salvage prostatectomy is associated with considerable morbidity, although 30 to 50% may be salvaged. Salvage brachytherapy appears to be associated with less morbidity and salvage rates of about 35%. The rationale of this study is to sensitize prostate cancer cells to radiation by injecting adenoviral-p53 vector directly into the prostate, allowing for enhanced cure rates using lower seed implant radiation doses. This strategy should reduce morbidity and enhance efficacy over salvage seed implant monotherapy.

Patient eligibility for the trial includes documented stage T1-T3 adenocarcinoma of the prostate prior to external beam radiotherapy. Failure after external beam radiotherapy would be evidenced by a rising PSA profile and a PSA doubling time of greater than one year. Post-external beam radiotherapy prostate biopsies must document recurrent adenocarcinoma of the prostate and the metastatic work up must be negative. The PSA at the time of failure must be less than or equal to 10 ng/ml and the prostate volume must be less than or equal to 55 cc. The strategy is for the intraprostatic injection of adenoviral-p53 three times while the 125-iodine seed radiation is active. The first intraprostatic injection would take place at the time of the seed implant and the next two injections would be spaced at two week intervals for a total of 3 intraprostatic adenoviral-p53 injections. From prior *in vitro* and *in vivo* tumor model studies, significant radiosensitization is expected by sequencing the treatments in this fashion.

A total of 74 patients will be entered into the trial, with 37 randomized to the treatment arm with adenoviral p53 plus 125-iodine seed implant versus 37 randomized to the arm with 125-iodine seed implant alone. The main end point of this study will be prostate biopsy at one year after completion of the treatment. A second biopsy will be performed at two years and PSA nadir levels will also be examined as a correlate of outcome.

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